How does the use of flavored nicotine vaping products relate to progression towards quitting smoking? Findings from the 2016 and 2018 ITC 4CV Surveys

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Abstract

Introduction: There is limited research on the role of flavors in nicotine vaping products (NVPs) in relation to smoking. We examined patterns of flavor use in NVPs in relation to progression towards quitting.

Methods: Data come from 886 concurrent users of NVPs (at least weekly) and cigarettes who were first surveyed in 2016 and then successfully recontacted in 2018 as part of the ITC 4CV Surveys conducted in Australia, Canada, England and the United States. Participants were asked about their main vaping flavor categorized as: 1) tobacco or unflavored, 2) menthol/mint flavored, and 3) "sweet" flavors (e.g., fruit/candy). We examined whether flavor was associated with progression towards quitting smoking between survey years.

Results: Overall, 11.1% of baseline concurrent users quit smoking by 2018. Compared to users of tobacco flavors, those vaping "sweet" flavors were more likely to quit smoking between surveys (13.8% vs. 9.6%; adjusted OR=1.61, 95% CI 1.01-2.58, p<0.05), but those using menthol flavors were no more likely to quit smoking (8.3% vs. 9.6%, aOR=0.87, 95% CI 0.43-1.47, p=0.69). Among those who had quit smoking in 2018, 52.0% were still vaping, which was lower than the 65.8% among continuing smokers (aOR=0.60, 95% CI 0.39-0.92, p=0.02). Sweet flavor users were no more likely to continue vaping compared to tobacco flavor users, either for those continuing smoking or those having quit smoking by 2018. There was a net shift away from tobacco flavor among those who continued to vape at follow-up.

Conclusions: Use of fruit and other sweet flavored e-liquids is positively related to smokers' transition away from cigarettes.

Implications

With multiple jurisdictions considering limiting or banning the sale of flavored NVPs, it is important to consider how such policies may impact smokers using NVPs to transition away from cigarette smoking. Our results indicate that vapers who used sweet flavors were more likely to transition away from cigarette smoking and quit cigarette use, at least in the short term, compared to those who used tobacco or unflavored NVPs. Randomized clinical trials are needed to establish if the observed association between use of flavored e-liquids and smoking cessation is due to self-selection or is truly causal.

Keywords: nicotine vaping products, flavors, smoking, concurrent use, smoking cessation

INTRODUCTION

With the growing popularity of nicotine vaping products (NVPs, also known as electronic cigarettes) among youth and young adults at least up to 2019 [1-7], there has been debate about whether NVPs will have a negative or positive net public health impact [6,8,9]. One aspect of this debate has been on how flavors make vaping attractive to non-smokers, especially youth [1,10-12]. Concern about flavors, commonly focuses on sweet flavors such as fruit and candy flavors, and to a lesser extent menthol and minty flavors, with tobacco flavorings generally ignored [6,13,14]. Concerns about flavors in NVPs appear to come from two broad possible mechanisms of effect. First, is concern that sweet flavors (such as fruit or candy) may encourage nonsmokers to initiate vaping [9,15-17]. Second, is a related concern that some flavors may mask the inherent aversiveness of inhaling nicotine which could lead those not dependent on nicotine to become dependent [6,15]. Among some researchers there is also concern that the toxicity of NVPs may be increased due to thermal degradation of flavor chemicals due to the heating [18]. However, this is unlikely to be a concern widely shared by consumers as use of unflavored vaping liquid appears to be low [19]. Both plausible mechanisms are theorized to increase the likelihood of both trial and continued use of vaping products, and thus continued exposure to nicotine [9,15,18]. Additionally there is concern that nonsmokers who begin vaping may transition to smoking [20]. On the other hand, advocates of vaping believe vaping is a pathway away from smoking as appealing NVP flavors are perceived as a positive product attribute because they could help lead smokers away from cigarettes[19,21]. For example, data from Canada and the United States (US) have shown that sweet flavors, such as fruit and candy, are reported by vapers as more satisfying than tobacco flavors [19].

If vaping flavors were found to have a beneficial effect on smoking cessation, such effects should be considered in policies and regulations on vaping flavors in combination with

evidence on their effect on non-smoking youth and young adults. Only a few studies have examined whether flavors in vaping products contribute to smoking cessation among adult smokers who also vape [22-25]. Cross-sectional data from Canada and the US [19] indicate that non-tobacco flavors, especially fruit, are popular among adult vapers, particularly among former smokers who are now exclusive vapers, suggesting they may play a role in cessation. Other population data from the US [26] indicated that tobacco is one of the most preferred flavors among adult smokers, although overall only a minority report using a tobacco flavor, as the range of flavors used is quite extensive depending on how they are grouped [26,27]. The most popular flavor category in England in 2019 was fruit flavor [28].

One UK cessation trial found that fruit was preferred among those who quit smoking (non-randomized comparison) [29]. A large online sample of adult vaping product consumers in the US also found that vapers who had completely switched from smoking cigarettes to NVPs were more likely to have initiated vaping with non-tobacco flavored e-liquid than those still smoking. The same study also found that many of those who quit with tobacco flavor reported transitioning to non-tobacco flavors over time [30].

The current study captures data on vaping behaviors among adults in four countries that differ in policies and regulations on NVPs – Australia, Canada, England, and the US. In Australia, NVPs with nicotine have always been banned for consumer use under pre-existing legislation [31], and there are no rules on flavors for non-nicotine vaping products. In Canada, vaping became federally regulated and legal for sale with nicotine in 2018, but the existing ban on nicotine vaping was widely unenforced at the time of our baseline survey (2016); since legalization, nicotine vaping is not approved for therapeutic use. In Canada, over the past decade, vaping specialty stores have increased their selection of devices and e-liquids with a range of nicotine strengths [32]. In England, NVPs and various attributes are regulated under the UK Tobacco and Related Products Regulations and are required to be notified to the

Medicines and Healthcare products Regulatory Agency (MHRA), which provides advice on the regulations governing content (including nicotine content and ingredients) and packaging. For example, maximum nicotine concentration for e-liquids is set at 20mg/ml (2016) [33], and some flavoring additives (e.g., diacetyl) have been prohibited. In the US, NVP advertising and sales are permitted in all channels and at the time of the surveys in 2016 and 2018, and there were no restrictions on flavors. In the US, labelling and advertisements are not permitted to include cessation claims or other medical/therapeutic claims [34]. These regulatory differences may further impact the degree to which NVPs and flavors are used in these countries.

Using longitudinal data from the 2016 and 2018 International Tobacco Control Four Country Smoking and Vaping (ITC 4CV) Surveys, we attempt to examine whether users of sweet flavors are more likely to quit smoking than users of tobacco flavors (in particular), and whether those quitting and continuing to vape would be more likely to move to sweet flavors than to tobacco flavors.

METHODS

Data source and participants

The ITC 4CV is an online survey conducted in Australia, Canada, England and the US. In addition to respondents retained from the ITC 4C Survey (the predecessor of the ITC 4CV Survey), adults (≥18 years) were recruited by commercial panel firms in each country as cigarette smokers, former smokers, and/or at-least-weekly vapers (total n=12,294 in 2016). All participants gave informed consent [35]. We started with 3081 at least weekly vapers who were asked about their NVP flavor use at the 2016 survey wave (Wave 1) and who provided valid data. Of these, 1174 were successfully recontacted in 2018 (Wave 2). This included 288 baseline exclusive vapers. Because only 34 of the exclusive vapers relapsed back to smoking

at Wave 2 (and only 25 continued vaping), there were not enough cases to do flavor specific analysis so they were excluded from the analytic sample. The final sample resulted in 886 baseline concurrent users with smoking status established at Wave 2 (Australia: n=69; Canada: n=371; England: n=249; US: n=197). Compared to those lost to follow-up, those retained were more likely to come from Canada and Australia, be older, of lower social economic status (SES), and were less likely to use sweet/menthol flavors or have plans to quit at baseline. In Supplementary Table 1 we compare this sample with those eligible respondents lost to follow-up. More details about the ITC 4CV Survey have been reported elsewhere [35-37].

Measures

Vaping Status

After screening for ever-use (with never or past use being coded as "no current use"), respondents were asked "*How often, if at all, do you currently use an NVP*?" (daily | less than daily, but at least once a week | less than weekly, but at least once a month | less than once a month, but occasionally | not at all | don't know). Only those who reported current vaping at least weekly were asked about the type of vaping product used, including the flavor of e-liquid used. Current vapers were further subdivided into those who vaped daily vs. those who vaped less than daily. For the longitudinal sample, their vaping status in 2018 was also coded as follows: daily, less than daily, but at least once a week, less than weekly (occasionally), or no longer vaping.

Use of NVP flavors

Current vapers were asked to indicate the main flavor used in the last month. Those reporting a main flavor (flavor most often used) were categorized into three groups: 1) tobacco or unflavored; 2) menthol or mint flavor, or 3) "sweet flavors" (which included 11 different flavor groups such as fruit flavor/candy, desserts, sweets/ chocolate/ clove or other spice/coffee/a non-alcoholic drink/an alcoholic drink/other flavor). We differentiated sweet flavors from menthol/mint flavors and tobacco/unflavored products because recent policies proposed to ban flavors exclude tobacco and in some cases menthol/mint flavors, whereas fruit and sweet flavors were most often slated for restrictions [6,38,39]. We also looked at reports of multiple flavor use (having used two or more flavor categories).

Cigarette smoking status

Cigarette smoking status was categorized as: current daily smokers, current weekly smokers, current monthly/< weekly smokers or recent quitters. In select analyses, a binary smoking level ("daily smokers" versus "non-daily smokers" (including currently weekly/monthly smokers)) was used.

A composite smoking and vaping measure (concurrent use) was computed based on Borland et al (2019) [40] with categories: "predominant smokers" (concurrent users who smoke daily and vape weekly); "dual daily" (both smoking and vaping daily); "concurrent non-daily" (smoke and vape less than daily); "predominant vapers" (vape daily, smoke less than daily). We also developed a measure of progression towards quitting smoking between waves based on the above measure with four categories: "stable"; "regress"; "progress, not quit"; and "quit smoking": "stable" refers to same frequency of use of both cigarettes and vaping; "regress" refers to smoking cigarettes at a higher frequency at Wave 2 compared to Wave 1 and "progress" refers to smoking at a lower frequency (e.g., from daily to weekly or

occasionally); and in the context of smoking the same frequency of cigarettes, vaping more frequently (e.g., weekly to daily) was categorized as "progress" as there is evidence that it increases likelihood of successful cessation [41,42], and vaping at lower frequency as "regress" for the purpose of this paper (also see Supplementary Table 2). For analyses focusing on smoking cessation, all three continuing smoker categories (regress, progress, and stable) were combined to compare with those quit smoking completely.

Other variables

Demographic measures used were gender (male, female) and age (18–24, 25–39, 40–54, 55 and older; and "<=39" vs. ">=40" in some analyses). Due to the differences in economic development and educational systems across countries, only relative levels of income and education were used. "Low" level of education referred to those who completed high school or less in Canada, the US, and Australia, or secondary/vocational or less in England; "moderate" meant community college/trade/technical school/some university (no degree) in Canada and the US, college/university (no degree) in England, or technical/trade/some university (no degree) in Australia; and "high" referred to those who completed university or postgraduate studies in all countries. Household income was also categorized into three levels ("low", "medium" and "higher"), with the tertiles roughly comparable across the four countries; and those who did not provide income information were included in the "not reported" group. Planning to quit smoking was asked among vapers who were currently smoking via the question "Are you planning to quit smoking?'. Response options were "within the next month", "within the next 6 months", "sometime in the future, beyond 6 months", and "not planning to quit/don't know". The first two categories were recoded as "yes, planning to quit within the next 6 months", and the remaining as "no current plans".

Data Analysis

Descriptive statistics (chi square tests) were used to examine sample characteristics by NVP flavor. To examine the association between flavor use and subsequent progression towards quitting smoking, both bivariable (unadjusted) and multivariable logistic regressions were employed, with the latter being adjusted for country, gender, age, education and income. We also tested for flavor by country interaction effects and separately flavor by age interaction effects, but did not retain interaction effects in the models because they were not significant. In addition, we looked at any possible differential loss to follow up by flavor at baseline. In all analyses, a p value <0.05 was considered statistically significant. All analyses were conducted using Stata Version 16.0.

RESULTS

Baseline sample characteristics and use of NVP flavors

Table 1 presents the sample characteristics by baseline flavor of NVPs. Overall, about 44% of the sample used tobacco flavor, 16% used menthol/mint, and another 40% used fruit and other flavors ("sweet flavors") at baseline. The preference for "sweet flavors" was particularly strong for those younger than 40 years compared to those who were older (OR=2.13, 95% CI 1.62-2.81, p<0.001) as well as for predominant vapers compared to predominant smokers (OR=1.99, 95% CI 1.27-3.11, p<0.01). Tobacco flavor was used more often by people aged 40 years and older compared to those who were under 40 years (OR=2.78, 95% CI 2.10-3.68, p<0.001). There was no difference in flavor preference by income, education or planning to quit smoking.

We also looked at reports of multiple flavor use in the last month, and found it was lowest among primary tobacco flavor users (30.7% at Wave 1 with another flavor); moderate among

menthol users (44.1%); and highest among users of "sweet" flavors (57.6%) even though this is only change outside the categories used (e.g., it misses shifts between sweet flavors).

The association of flavor and progression towards quitting smoking

Tables 2 and 3 show the longitudinal results among 886 concurrent vapers followed between Wave 1 and Wave 2. Overall, 11.1% of concurrent users quit smoking by 2018. Compared to tobacco flavor users, concurrent users using "sweet" flavors in 2016 were more likely to have quit smoking by 2018 (13.8% vs 9.6%, adjusted OR=1.61, 95% CI 1.01-2.58, p<0.05); but those using menthol flavor were no more likely to quit (8.3% vs 9.6%, aOR=0.87, 95% CI 0.43-1.74, p=0.69). Regression results show that neither age, nor gender (or other sociodemographic variables) independently predicted higher cessation rates (all p-values >0.05, see Table 3 for details). The analysis included controls for key variables with differential retention including age and flavor use at baseline. In supplementary analysis, we checked the cessation rates of baseline daily vapers vs. weekly vapers and found they were not significantly different (12.9% vs 9.2%, OR=1.45, 95% CI 0.95-2.22, p=0.08). Given the trend in further analyses, we included the vaping frequency variable (daily vs. weekly) in the regressions. It had essentially the same trend as independently, and had a small effect on the flavor relationship, but notably moving it to just above the criterion significance (p=0.06). Reporting of progression (but not quit smoking) was similar among the three flavor user groups (tobacco flavor: 19.9%; sweet flavors: 20.9%; menthol flavors: 21.4%, Table 2).

Among those who continued smoking at 2018 (n=783), 65.8% were still vaping at least weekly at Wave 2. No differences were found in percent still using by the vaping flavor reported: 66.7% used tobacco flavor compared to 65.4% using menthol (aOR=0.85, 95% CI 0.55-1.33, p=0.49), and tobacco flavor compared to 64.9% using sweet flavors (aOR=0.82, 95% CI 0.58-1.16, p=0.26). Among those who had quit smoking in 2018 (n=98), 52.0% were

still vaping (which was lower than 65.8% among those who continued smoking, aOR=0.60, 95% CI 0.39-0.92, p=0.02). There was no difference in continuing vaping by flavor used at baseline: tobacco flavor (59.5%) vs sweet flavor users (53.1%, aOR=1.06, 95% CI 0.34-3.32, p=0.92).

Finally, we explored flavor transitions to and from tobacco flavor. Overall, there was more movement away from tobacco to any other flavors (28.3%) than to tobacco from other flavors (20.2%, p<0.05). Those who quit smoking and continued vaping were less likely to switch from tobacco flavor than those still smoking (18.2% vs 29.3%, p<0.05). There was no evidence of any interaction.

DISCUSSION

This study aimed to examine patterns of flavor use in NVPs in relation to progression towards quitting smoking. Overall, 11.1% of concurrent users quit smoking by 2018, which is similar to that among exclusive smokers in the same data set [43]. As we predicted, the data showed that smokers using "sweet" flavored NVPs were more likely to quit smoking compared to those using tobacco/unflavored NVPs, but this was not the case for menthol/mint. Among those who continued smoking at follow-up, two-thirds were still vaping at least weekly, but there were no differences in percent still using by vaping flavors. Among those who had quit smoking by follow-up, half were still vaping, and again, there were no differences between flavors. Overall, there was a net shift away from tobacco flavor among those who continued to vape at follow-up. It is also worth noting that there were no differences in flavor preference by reported plans to quit at baseline. Tobacco flavor was more likely to be used by older vapers. Consistent with previous research [15,26], users of tobacco flavor were least likely to use other flavor types (i.e., to use multiple flavors).

The above results are consistent with sweet flavors facilitating quitting compared to tobacco flavor, but it is premature to claim any causality for flavors in smoking cessation. It is important to find out whether banning fruit and other sweet flavors might reduce quitting, or whether those who prefer sweet flavors would simply switch to menthol or tobacco flavored e-liquids and quit at the same rates. Even if it did not facilitate quitting when used, if more smokers were prepared to use sweet flavors and use them regularly (e.g., daily), and even if vaping sweet flavors does lead to increased quitting, it could also have an indirect positive effect; that is, some loss of smoking cessation potential due to reduced desirability of vaping, and hence less frequent and sustained use to try to quit.

If use of sweet vaping flavors is more desirable (as was shown in Gravely et al [19]) it might also influence reducing relapse by being more likely to continue use than for a less attractive product. Frequent and sustained use over time has been shown with other nicotine substitutes to increase quitting [44]. It is also conceivable that the much more distinct differences between sweet flavors and the taste of smoking may favor maintenance of quit attempts. Relevant to this, a recent animal study reported that the addition of fruit flavor to e-liquid increased nicotine self-administration with the result being synergistic for the combination of nicotine and fruit flavor [45]. This may suggest for some, vaping fruit flavors could be an overall superior experience to smoking tobacco, which should make it protective from returning to smoking. The finding of a net drift away from use of tobacco flavor, replicating previous work [19,30], is suggestive of a net desire for vaping to be seen as an activity more distinct from smoking, but we do not have anywhere near enough cases of shifting to ascertain whether this is playing any role in smoking cessation. The finding that those who quit smoking with tobacco flavor were less likely to have switched than those who remained smoking is harder to interpret. It could be that the continuing smokers are looking for an alternative that might help them to quit, or are treating vaping as a parallel experience. Once quit, they may see less

need to switch. Whether this will result in them being more or less likely to continue to vape is uncertain as is any possible effect on relapse proneness.

There are several limitations to this study that should be acknowledged. First, the flavor options we allowed respondents to choose from were limited and in some cases do not capture the specific flavors preferred. For example, fruit and candy e-liquid flavors are diverse, so use of multiple flavors within such categories could not be detected. Given that we found more between category shifting for those reporting one of the sweet flavors, it suggests that the real differences in shifting may be even larger; that is, the majority of sweet flavor users use multiple flavors while tobacco and non-flavor users tend to stay with the one flavor. Second, the time frame for flavor use was only the past 30 days and this may not reflect longer term patterns, although our longitudinal data gives some idea of stability over time. Third, our study was not able to examine the role of different vaping flavors during specific smoking quit attempts. Fourth, our analyses are unable to control for NVP types or nicotine levels of the vaping liquid, so we are limited in what we can say about variability in flavor use by type of device or nicotine levels and whether these could have contributed to the observed differences. Fifth, it should be noted that although the cessation rates of daily vapers were not statistically higher than weekly vapers, there was a positive trend consistent with studies that have found higher cessation rates for daily vapers compared to those who vape less than daily [41,42]. Further, we cannot say whether the differential levels of quitting reflect increases in one group or decreases in the other, but given that those who vape to quit are typically more dependent [46,47], this is not really relevant. It should also be noted that the study relies on self-report data which may not be reliable. However, we cannot see any reason why there would be differential mis-reporting between those using different flavored e-liquids. Some caution is required given the differential pattern of attrition, but as we mentioned earlier that we were able to control for variables with differential attrition, the

flavor effects were robust, making it less likely that differential attrition is responsible for the findings.

Strengths of the study include the longitudinal design of the study, multi-country data, and sufficient sample to allow us to identify moderate associations between flavor use and outcomes of interest. However, we acknowledge that randomized clinical trials would be needed to establish definitively if the observed association between use of different vaping flavors and smoking cessation is due to self-selection or is truly causal. If flavors are banned in some jurisdictions, it might allow natural experiments to better understand their roles.

In conclusion, vapers' use of fruit and other sweet flavored e-liquids was positively related to quitting smoking by follow-up. However, among continued concurrent use, there were no differences in percent still vaping by flavors used. This study also found that more vapers transitioned from tobacco to other flavors by follow-up than the reverse, although overall switching was lower in vapers who had quit smoking. We think it possible that limiting smokers' access to fruit and other sweet vaping flavors may have an overall negative impact on quitting, but this is far from definitive.

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References

1. Cullen KA, Gentzke AS, Sawdey MD, et al. e-Cigarette Use Among Youth in the United States, 2019. *JAMA.* 2019;322(21):2095-2103.
2. Hammond D, Reid JL, Rynard VL, et al. Prevalence of vaping and smoking among adolescents in Canada, England, and the United States: repeat national cross sectional surveys. *BMJ.* 2019;365:l2219.
3. Villanti AC, Feirman SP, Niaura RS, et al. How do we determine the impact of e-cigarettes on cigarette smoking cessation or reduction? Review and recommendations for answering the research question with scientific rigor. *Addiction.* 2018;113(3):391-404.
4. Harrell MB, Weaver SR, Loukas A, et al. Flavored e-cigarette use: Characterizing youth, young adult, and adult users. *Prev Med Rep.* 2017;5:33-40.
5. Hammond D, Rynard V, Reid J. Changes in prevalence of vaping among youth in the United States, Canada, and England, 2017 to 2019. *JAMA Pediatr (in press).*
6. Goldenson NI, Leventhal AM, Simpson KA, Barrington-Trimis JL. A Review of the Use and Appeal of Flavored Electronic Cigarettes. *Curr Addict Rep.* 2019;6(2):98-113.
7. Jones DM, Ashley DL, Weaver SR, Eriksen MP. Flavored ENDS Use among Adults Who Have Used Cigarettes and ENDS, 2016-2017. *Tob Regul Sci.* 2019;5(6):518-531.
8. Mendez D, Warner KE. A magic bullet? The potential impact of e-cigarettes on the toll of cigarette smoking. *Nicotine Tob Res.* 2020 (Aug 21:ntaa160. doi: 10.1093/ntr/ntaa160. Epub ahead of print).
9. Meernik C, Baker HM, Kowitt SD, Ranney LM, Goldstein AO. Impact of non-menthol flavours in e-cigarettes on perceptions and use: an updated systematic review. *BMJ Open*. 2019;9(10):e031598.
10. Gilley M, Beno S. Vaping implications for children and youth. *Curr Opin Pediatr.* 2020;32(3):343-348.
11. Singh S, Windle SB, Filion KB, et al. E-cigarettes and youth: Patterns of use, potential harms, and recommendations. *Prev Med.* 2020;133:106009.
12. Soneji SS, Knutzen KE, Villanti AC. Use of Flavored E-Cigarettes Among Adolescents, Young Adults, and Older Adults: Findings From the Population Assessment for Tobacco and Health Study. *Public Health Rep.* 2019;134(3):282-292.
13. Harvanko A, Kryscio R, Martin C, Kelly T. Stimulus effects of propylene glycol and vegetable glycerin in electronic cigarette liquids. *Drug Alcohol Depend.* 2019;194:326-329.
14. Rao PD, Nanding H, Strasser AA, Wise PM. Pilot Experiment: The Effect of Added Flavorants on the Taste and Pleasantness of Mixtures of Glycerol and Propylene Glycol. *Chemosens Percept.* 2018;11(1):1-9.
15. Zare S, Nemati M, Zheng Y. A systematic review of consumer preference for e-cigarette attributes: Flavor, nicotine strength, and type. *PLOS ONE.* 2018;13(3):e0194145.
16. Kong G, Morean ME, Cavallo DA, Camenga DR, Krishnan-Sarin S. Reasons for Electronic Cigarette Experimentation and Discontinuation Among Adolescents and Young Adults. *Nicotine Tob Res.* 2015;17(7):847-854.
17. Pepper JK, Ribisl KM, Brewer NT. Adolescents' interest in trying flavoured e-cigarettes. *Tob Control*. 2016;25(Suppl 2):ii62-ii66.
18. Leventhal AM, Goldenson NI, Cho J, et al. Flavored E-cigarette Use and Progression of Vaping in Adolescents. *Pediatrics*. 2019;144(5):e20190789.
19. Gravely S, Cummings KM, Hammond D, et al. The association of e-cigarette flavors with satisfaction, enjoyment, and trying to quit or stay abstinent from smoking among regular adult vapers from Canada and the United States: Findings from the 2018 ITC Four Country Smoking and Vaping Survey. *Nicotine Tob Res.* 2020;22(10):1831-1841. doi: 10.1093/ntr/ntaa095.

20. Khouja JN, Suddell SF, Peters SE, Taylor AE, Munafò MR. Is e-cigarette use in non-smoking young adults associated with later smoking? A systematic review and meta-analysis. *Tob control.* 2020 (Mar 10:tobaccocontrol-2019-055433. doi: 10.1136/tobaccocontrol-2019-055433. Epub ahead of print).
21. Warner KE, Mendez D. E-cigarettes: Comparing the Possible Risks of Increasing Smoking Initiation with the Potential Benefits of Increasing Smoking Cessation. *Nicotine Tob Res.* 2019;21(1):41-47.
22. Yong HH, Borland R, Cummings KM, et al. Reasons for regular vaping and for its discontinuation among smokers and recent ex-smokers: findings from the 2016 ITC Four Country Smoking and Vaping Survey. *Addiction.* 2019;114 Suppl 1:35-48.
23. Camenga DR, Kong G, Cavallo DA, Krishnan-Sarin S. Current and Former Smokers' Use of Electronic Cigarettes for Quitting Smoking: An Exploratory Study of Adolescents and Young Adults. *Nicotine Tob Res.* 2016;19(12):1531-1535.
24. Czoli CD, Goniewicz M, Islam T, Kotnowski K, Hammond D. Consumer preferences for electronic cigarettes: results from a discrete choice experiment. *Tob Control.* 2016;25(e1):e30-e36.
25. Friedman AS, Xu S. Associations of Flavored e-Cigarette Uptake With Subsequent Smoking Initiation and Cessation. *JAMA Netw Open.* 2020;3(6):e203826.
26. Schneller LM, Bansal-Travers M, Goniewicz ML, McIntosh S, Ossip D, O'Connor RJ. Use of Flavored E-Cigarettes and the Type of E-Cigarette Devices Used among Adults and Youth in the US—Results from Wave 3 of the Population Assessment of Tobacco and Health Study (2015–2016). *Int J Environ Res Public Health.* 2019;16(16):2991.
27. Zhu S-H, Sun JY, Bonnevie E, et al. Four hundred and sixty brands of e-cigarettes and counting: implications for product regulation. *Tob Control*. 2014;23(suppl 3):iii3-iii9.
28. McNeill A, Brose L, Calder R, Bauld L, Robson D. *Vaping in England: an evidence update including mental health and pregnancy, March 2020: A report commissioned by Public Health England.* London: Public Health England. 2020.
29. Hajek P, Phillips-Waller A, Przulj D, et al. A Randomized Trial of E-Cigarettes versus Nicotine-Replacement Therapy. *N Engl J Med.* 2019;380(7):629-637.
30. Russell C, McKeganey N, Dickson T, Nides M. Changing patterns of first e-cigarette flavor used and current flavors used by 20,836 adult frequent e-cigarette users in the USA. *Harm Reduct J.* 2018;15(1):33.
31. Greenhalgh E, Scollo M, Winstanley M. *Tobacco in Australia: Facts and issues. Melbourne: Cancer Council Victoria; 2020. Available from https://www.tobaccoinaustralia.org.au/home.aspx.* 2020.
32. Braak DC, Cummings KM, Nahhas GJ, et al. Where Do Vapers Buy Their Vaping Supplies? Findings from the International Tobacco Control (ITC) 4 Country Smoking and Vaping Survey. *Int J Environ Res Public Health* 2019;16:338.
33. Medicines and Healthcare products Regulatory Agency (MHRA). Guidance: E-cigarettes: regulations for consumer products. Accessed on February 17, 2020. Available at: https://www.gov.uk/guidance/e-cigarettes-regulations-for-consumer-products. In:2016.
34. US Food & Drug Administration. FDA's Deeming Regulations for E-Cigarettes, Cigars, and All Other Tobacco Products: https://www.fda.gov/tobacco-products/rules-regulations-and-guidance/fdas-deeming-regulations-e-cigarettes-cigars-and-all-other-tobacco-products. 2019. Accessed March 26, 2020.
35. Thompson ME, Fong GT, Boudreau C, et al. Methods of the ITC Four Country Smoking and Vaping Survey, wave 1 (2016). *Addiction.* 2019;114 Suppl 1:6-14.
36. Thompson ME, Fong GT, Hammond D, et al. Methods of the International Tobacco Control (ITC) four country survey. *Tob control.* 2006;15(suppl 3):iii12-iii18.
37. ITC Project. *ITC Four Country Smoking and Vaping Survey, Wave 2 (2018) Technical Report.* . University of Waterloo, Waterloo, Ontario, Canada; Medical University of South Carolina,

Charleston, South Carolina, United States; Cancer Council Victoria, Melbourne, Australia; the University of Queensland, Australia; King's College London, London, United Kingdom.2020, January.
38. Health NCfCDPaHPUOoSa. *E-Cigarette Use Among Youth and Young Adults: A Report of the Surgeon General [Internet]. Chapter 1, Introduction, Conclusions, and Historical Background Relative to E-Cigarettes. Available from: https://www.ncbi.nlm.nih.gov/books/NBK538684/.* Atlanta (GA): Centers for Disease Control and Prevention (US); 2016.
39. Villanti AC, Johnson AL, Glasser AM, et al. Association of Flavored Tobacco Use With Tobacco Initiation and Subsequent Use Among US Youth and Adults, 2013-2015. *JAMA Netw Open.* 2019;2(10):e1913804.
40. Borland R, Murray K, Gravely S, et al. A new classification system for describing concurrent use of nicotine vaping products alongside cigarettes (so-called 'dual use'): findings from the ITC-4 Country Smoking and Vaping wave 1 Survey. *Addiction.* 2019;114 Suppl 1:24-34.
41. Giovenco DP, Delnevo CD. Prevalence of population smoking cessation by electronic cigarette use status in a national sample of recent smokers. *Addict Behav.* 2018;76:129-134.
42. Berry KM, Reynolds LM, Collins JM, et al. E-cigarette initiation and associated changes in smoking cessation and reduction: the Population Assessment of Tobacco and Health Study, 2013-2015. *Tob control.* 2019;28(1):42-49.
43. Gravely S, Meng G, Cummings KM, et al. Changes in Smoking and Vaping over 18 Months among Smokers and Recent Ex-Smokers: Longitudinal Findings from the 2016 and 2018 ITC Four Country Smoking and Vaping Surveys. *Int J Environ Res Public Health.* 2020;17(19).
44. Hartmann‐Boyce J, Chepkin SC, Ye W, Bullen C, Lancaster T. Nicotine replacement therapy versus control for smoking cessation. *Cochrane Database Syst Rev.* 2018(5).
45. Wong AL, McElroy SM, Robinson JM, et al. Flavor-specific enhancement of electronic cigarette liquid consumption and preference in mice. *Drug Alcohol Depend.* 2020;211:107995.
46. Selya AS, Dierker L, Rose JS, Hedeker D, Mermelstein RJ. The Role of Nicotine Dependence in E-Cigarettes' Potential for Smoking Reduction. *Nicotine Tob Res.* 2017;20(10):1272-1277.
47. Berry KM, Reynolds LM, Collins JM, et al. E-cigarette initiation and associated changes in smoking cessation and reduction: the Population Assessment of Tobacco and Health Study, 2013–2015. *Tob Control.* 2019;28(1):42-49.

Table 1. Sample characteristics, by baseline flavor of vaping products.

	Overall	Tobacco or unflavored#	Menthol/mint	Sweet flavor
	N^	(n=387) %	(n=145) %	(n=354) %
Total	886 (100%)	43.7	16.4	39.9
Country	*			
Canada	371	41.8	14.0	44.2
US	197	38.6	21.8	39.6
England	249	48.2	15.3	36.5
Australia	69	52.2	17.4	30.4
Gender	*			
Male	475	47.4	14.5	38.1
Female	411	39.4	18.5	42.1
Age group	***			
18-24	142	24.7	18.3	57.0
25-39	240	32.9	20.8	46.2
40-54	255	53.7	13.3	32.9
>=55	249	54.6	14.1	31.3
Education	N.S			
Low	240	46.3	15.8	37.9
Moderate	354	43.5	16.4	40.1
High	292	41.8	16.8	41.4
Income	N.S			
Low	221	42.5	16.7	40.7
Moderate	282	44.0	13.1	42.9
High	345	44.9	18.0	37.1
Not reported	38	36.8	23.7	39.5
Smoking & vaping categories	**			

Predominant smokers (smoke daily and vape weekly)	359	49.0	14.8	36.2
Dual daily users	333	45.4	17.1	37.5
Predominant vapers (vape daily and smoke<daily)	100	28.0	19.0	53.0
Concurrent non-daily(weekly)	94	34.0	17.0	48.9
Planning to quit	N.S			
Yes##	413	42.1	17.0	40.9
No	472	45.1	15.9	39.0

^In some analyses the numbers were less than the total due to missing cases. #This refers to the flavor a participant used most (if s/he used more than one flavor). * Significant at p<0.05; ** significant at p<0.01; *** significant at p<0.001 based on chi square tests; N.S: Not significant.

Table 2. Transition away or toward smoking cigarettes from 2016 to 2018, by baseline flavor^

		Wave 1 flavor (2016)			
Wave 2 (2018) status	N	**Tobacco or unflavored** (n=387), 43.7%	**Menthol/mint** (n=145),16.3%	**Sweet flavor** (n=354), 40%	**Total** (n=886), 100%
Quit smoking (*and vaping status at Wave 2***)**	**98**	**9.6**	**8.3**	**13.8**	**11.1**
- Stopped vaping (no vaping)	47	3.9	6.2	6.5	5.3
- Still vaping (vaping)	51	5.7	2.1	7.3	5.8
Still smoking#	**788**	**90.4**	**91.7**	**86.2**	**88.9**
- Progress but not quit	182	19.9	21.4	20.9	20.5
- Stable	248	31.3	29.0	24.0	28.0
- Regress##	358	39.3	41.4	41.2	40.4
Vaping status among continuing smokers	*783*	*N=348*	*N=133*	*N=302*	*N=783*
- Stopped vaping	268	33.3	34.6	35.1	34.2
- Vaping	515	66.7	65.4	64.9	65.8

^The analyses reported in this table were on unweighted data. #In some longitudinal analyses all three continuing smoker categories were combined to compare with those quit smoking. ##This refers to smoking cigarettes at a higher frequency at Wave 2 compared to Wave 1; whereas "progress, but not quit" refers to reduced smoking.

Table 3. The association between baseline flavor use/characteristics and quitting outcome at follow up (n=886)

Factors	n	% Quit	Adjusted OR	95% CI
Baseline flavor^				
Tobacco	387	9.6	Ref#	
Menthol	145	8.3	0.87	0.43-1.74
Sweet	354	13.8	1.61	1.01-2.58*
Country				
Canada	371	11.6	Ref	
US	197	12.2	1.03	0.59-1.77
England	249	8.8	0.75	0.43-1.29
Australia	69	13.0	1.13	0.51-2.49
Gender				
Male	475	9.9	Ref	
Female	411	12.4	1.26	0.82-1.93
Age				
<=39 years	382	9.9	Ref	
40 years+	504	11.9	1.33	0.84-2.09
Education				
Low	240	11.7	Ref	
Moderate	354	10.7	0.89	0.52-1.53
High	292	11.0	0.92	0.51-1.67
Income				
Low	221	11.3	Ref	
Moderate	282	9.9	0.89	0.49-1.59
High	345	12.2	1.15	0.65-2.05
Not reported	38	7.9	0.69	0.19-2.44

^We tested for flavor by country interaction effects (and flavor by age effects) and found the interaction terms were not significant, therefore the interactions terms were not included in the final model. The results presented in this table are for all four countries. OR: Odds ratio, CI: confidence interval; adjusted for country, gender, age, education and income #Ref: reference value. * Significant at $p<0.05$; ** significant at $p<0.01$; *** significant at $p<0.001$.